This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1. (Currently amended) A formulation comprising a gas microsphere liposome composite suspended in a medium, wherein the gas microsphere liposome composite comprises:

a gas-filled microsphere;

at least one of a lipid and a surfactant adsorbed onto the surface of the gas-filled microsphere; ~~and~~

liquid-filled liposomes attached to the lipid or surfactant~~, wherein each of the liquid-filled liposomes independently has a diameter of about 20nm to about 100nm~~ ; and

high affinity targeting moieties attached to at least one of said lipid, said surfactant, or said liquid-filled liposomes, said high affinity targeting moieties selected from the group consisting of:

1,2-dipalmitoyl-*sn*-glycero-3-phosphoethanolamine-cyclo(Arg-Gly-Asp-D-Phe-Lys)-dodecanoate;

DPPE-PEG_{3400}-cyclo(Arg-Gly-Asp-D-Phe-Lys)-dodecanoate;

1-(1,2-Dipalmitoyl-*sn*-glycero-3-phosphoethanolamino)-α,ω-dicarbonyl PEG_{3400}-2-{[7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]carbonylamino}-N-(3-aminopropyl)acetamide; and

1-(1,2-Dipalmitoyl-*sn*-glycero-3-phosphoethanolamino)-α,ω-dicarbonyl PEG_{3400}-[7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]-N-{[4-(aminomethyl)phenyl]methyl}carboxamide.

2. (Original) The formulation of claim 1 wherein the gas of the gas-filled microsphere has a solubility of less than about 1.0% (v/v) in water at 25°C and 1 atm.

3. (Original) The formulation of claim 1 wherein the gas-filled microsphere has an average diameter of about 0.1μm to about 10μm.

4. (Original) The formulation of claim 1 wherein the gas-filled microsphere has an average diameter of about 0.5μm to about 10μm.

5. (Original) The formulation of claim 1 wherein the gas-filled microsphere comprises at least one inert gas.

6. (Original) The formulation of claim 5 wherein the inert gas is a noble gas.

7. (Original) The formulation of claim 5 wherein the inert gas is a perfluoroether gas.

8. (Original) The formulation of claim 5 wherein the inert gas is a perfluorocarbon gas.

9. (Original) The formulation of claim 1 wherein the gas-filled microsphere has a lipid adsorbed onto the surface of the gas-filled microsphere.

10. (Original) The formulation of claim 1 wherein the gas-filled microsphere has a surfactant adsorbed onto the surface of the gas-filled microsphere.

11. (Original) The formulation of claim 1 wherein the lipid or surfactant forms a mono-molecular layer on the surface of the gas-filled microsphere.

12. (Original) The formulation of claim 1 wherein the lipid or surfactant forms a bi-molecular liposomal layer or multi-molecular liposomal layer on the surface of the gas-filled microsphere.

13. (Original) The formulation of claim 1 wherein the surfactant is a non-ionic surfactant, cationic surfactant, or anionic surfactant.

14. (Currently amended) The formulation of claim 13 wherein the non-ionic surfactant comprises polyethylene glycol, polypropylene glycol, ~~polyvinylpyrollidone~~ polyvinylpyrrolidone, polyvinylalcohol, cellulose, gelatin, xanthan gum, pectin, or dextran.

15. (Original) The formulation of claim 13 wherein the cationic surfactant comprises a tetraalkyl ammonium, tetraalkyl phosphonium ion, or a suitable salt thereof.

16. (Original) The formulation of claim 15 wherein the cationic surfactant comprises a tetrahexyl ammonium, tetraoctyl ammonium, tetradecyl ammonium, tetrabutyl ammonium, tetrahexyl phosphonium, tetraoctyl phosphonium, tetrabutyl phosphonium, tetraphenyl phosphonium, or a suitable salt thereof.

17. (Original) The formulation of claim 13 wherein the anionic surfactant comprises an alkyl sulfonate, an alkyl carboxylate, or a suitable salt thereof.

18. (Original) The formulation of claim 17 wherein the anionic surfactant comprises dodecyl sulfate, palmityl sulfate, dodecyl carboxylate, palmityl carboxylate, or a suitable salt thereof.

19. (Original) The formulation of claim 1 wherein the lipid comprises a phospholipid, glycolipid, triglyceride or fatty acid.

20. (Original) The formulation of claim 19 wherein the phospholipid comprises dipalmitoylphosphatidyl choline, dimyristoylphosphatidyl choline, dilauryoylphosphatidyl choline, or dioleoylphosphatidyl choline.

21. (Original) The formulation of claim 1 wherein the liquid-filled liposomes are attached to the adsorbed lipid or surfactant in a continuous fashion.

22. (Original) The formulation of claim 1 wherein the liquid-filled liposomes occupy greater than about 50% of the outer surface of the gas-filled microsphere area.

23. (Original) The formulation of claim 1 wherein each of the liquid-filled liposomes independently has a diameter of about 10nm to about 200nm.

24. (Canceled).

25. (Original) The formulation of claim 1 wherein each of the liquid-filled liposomes independently has a diameter that is less than about 10% of the diameter of the gas-filled microsphere.

26. (Original) The formulation of claim 1 wherein each of the liquid-filled liposomes independently comprises a therapeutic agent or diagnostic agent in the interior of the liquid-filled liposomes.

27. (Original) The formulation of claim 26 wherein the therapeutic agent is an anticoagulant, thrombolytic, antineoplastic agent, or anti-inflammatory agent.

28. (Currently amended) The formulation of claim 26 wherein the therapeutic agent comprises doxorubicin, cyclophosphamide, adriamycin, methotrexate, gemcitabine, navelbine, cisplatin, tissue plasminogen activator, integrelin, roxifiban~~, methotrexate~~ or enbrel.

29. (Original) The formulation of claim 26 wherein the diagnostic agent comprises an X-ray contrast agent or an MRI contrast agent.

30. (Currently amended) The formulation of claim 1 wherein each of the liquid-filled liposomes independently has high affinity, targeting moieties attached to the surface ~~of the liquid-filled liposomes~~ thereof.

31-33. (Canceled)

34. (Original) The formulation of claim 1 wherein each of the liquid-filled liposomes independently comprises liquid from the medium of suspension.

35. (Original) The formulation of claim 1 wherein the gas microsphere liposome composite has a mean diameter of about 0.1μm to about 10μm.

36. (Original) The formulation of claim 1 wherein the gas microsphere liposome composite has a mean diameter of about 0.2μm to about 4μm.

37. (Original) The formulation of claim 1 wherein the gas microsphere liposome composite exists as an aggregate of two or more gas microsphere liposome composites.

38. (Original) The formulation of claim 37 wherein the aggregate has a diameter of about 1μm to about 100μm.

39. (Original) The formulation of claim 1 wherein the gas microsphere liposome composite has a density of about 0.90 to about 1.10 of the density of the medium.

40. (Original) The formulation of claim 1 wherein the lipid or surfactant comprises a high affinity targeting moiety.

41. (Original) The formulation of claim 1 wherein the lipid or surfactant comprises a therapeutic agent.

42. (Currently amended) The formulation of claim 41 wherein the therapeutic agent is doxorubicin, cyclophosphamide, adriamycin, methotrexate, gemcitabine, navelbine, cisplatin, tissue plasminogen activator, integrelin, roxifiban~~, methotrexate~~ or enbrel.

43. (Original) The formulation of claim 1 wherein the medium comprises a diagnostic agent.

44. (Original) The formulation of claim 43 wherein the diagnostic agent is an X-ray or MRI contrast agent.

45. (Canceled)

46. (Previously amended) A method of ultrasound imaging in a patient in need of such ultrasound imaging comprising:

administering to the patient an effective amount of a formulation of claim 1;

allowing a sufficient period of time for the circulation of the gas microsphere composite to reach the targeted area; and

performing ultrasound imaging on the patient.

47. (Original) The method of claim 46 wherein the patient is a human.

48. (Original) The method of claim 46 wherein the effective amount of the formulation comprises about 10^3 to about 10^{10} gas microsphere liposome composites.

49. (Original) The method of claim 46 wherein the sufficient period of time is about 5 minutes to about 2 hours.

50. (Original) The method of claim 46 wherein the sufficient period of time is about 5 to about 30 minutes.

51. (Previously amended) A method of treating heart disease, inflammation, infection, cancer or thromboembolic disease in a patient in need of such treatment comprising:

administering to the patient an effective amount of a formulation of claim 1, wherein one or more of the liquid-filled liposomes independently comprises a therapeutic agent;

allowing a sufficient period of time for the circulation of the gas microsphere composite to the targeted area; and

applying ultrasound energy to the region of pathology in the patient sufficient to cause the therapeutic agent to be released from the microsphere liposome composite at the region of pathology.

52. (Original) The method of claim 51 wherein the patient is a human.

53. (Original) The method of claim 51 wherein each of the liquid-filled liposomes independently comprises a therapeutic agent.

54. (Original) The method of claim 51 wherein the effective amount of the formulation comprises about 10^3 to about 10^{10} gas microsphere liposome composites.

55 to 68. (Canceled)

69. (Currently amended) A formulation comprising a gas microsphere liposome composite suspended in a medium, wherein the gas microsphere liposome composite comprises:

a gas-filled microsphere;

at least one of a lipid and a surfactant adsorbed onto the surface of the gas-filled microsphere; ~~and~~

liquid-filled liposomes attached to the lipid or surfactant; and

high affinity targeting moieties attached to said lipid, said surfactant, or said liquid-filled liposomes, said high affinity targeting moieties selected from the group consisting of:

1,2-dipalmitoyl-*sn*-glycero-3-phosphoethanolamine-cyclo(Arg-Gly-Asp-D-Phe-Lys)-dodecanoate;

DPPE-PEG_{3400}-cyclo(Arg-Gly-Asp-D-Phe-Lys)-dodecanoate;

1-(1,2-Dipalmitoyl-*sn*-glycero-3-phosphoethanolamino)-α,ω-dicarbonyl PEG_{3400}-2-{[7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]carbonylamino}-N-(3-aminopropyl)acetamide; and

1-(1,2-Dipalmitoyl-*sn*-glycero-3-phosphoethanolamino)-α,ω-dicarbonyl PEG_{3400}-[7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]-N-{[4-(aminomethyl)phenyl]methyl}carboxamide;

for use in medical therapy or diagnosis~~, wherein each of the liquid-filled liposomes independently has a diameter of about 20nm to about 100nm~~.

70 to 72. (Canceled).

73. (New) The formulation of claim 23, wherein each of the liquid-filled liposomes has a diameter of about 20 nm to about 100 nm.

74. (New) The formulation of claim 69, wherein each of the liquid-filled liposomes has a diameter of about 20 nm to about 100 nm.